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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *
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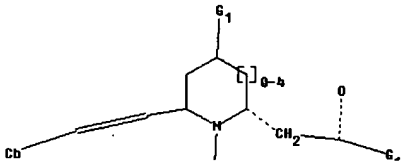

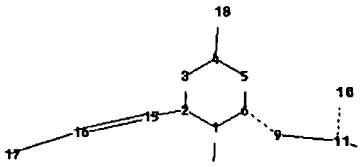


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chain nodes :
9  10  11  13  15  16  17  18  20
ring nodes :
1  2  3  4  5  6
chain bonds :
1-20  2-15  4-18  6-9  9-11  10-11  11-13  15-16  16-17
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  1-20  2-3  3-4  4-5  4-18  5-6  6-9  10-11  11-13
exact bonds :
2-15  9-11  15-16  16-17
isolated ring systems :
containing 1 :


G1:Ak,H,Cb

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  9:CLASS  10:CLASS  11:CLASS
13:CLASS  15:CLASS  16:CLASS  17:Atom  18:CLASS  20:CLASS



L1      STRUCTURE UPLOADED

=> dis l1
L1 HAS NO ANSWERS
L1              STR
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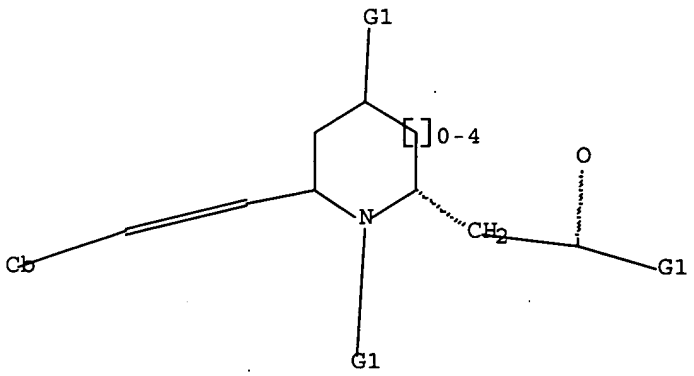

G1 Ak,H,Cb

Structure attributes must be viewed using STN Express query preparation.

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L2             1 SEA SSS SAM L1

=> s  l1 full
L3             9 SEA SSS FUL L1

=> file caplus
=> s L3
L4             4 L3

=> s l4 and pd<july 1999
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                  (PD<19990700)
L5             1 L4 AND PD<JULY 1999

=> dis bib abs hitstr

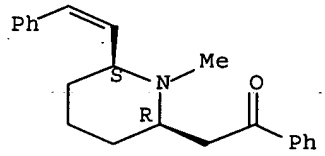
L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   1999:510839  CAPLUS Full-text
DN   131:281005
TI   Lobeline: Structure-Affinity Investigation of Nicotinic Acetylcholinergic
     Receptor Binding
AU   Flammia, Dwight; Dukat, Malgorzata; Damaj, M. Imad; Martin, Billy;
     Glennon, Richard A.
CS   Department of Medicinal Chemistry School of Pharmacy and Department of
     Pharmacology and Toxicology School of Medicine, Virginia Commonwealth
     University, Richmond, VA, 23298-0540, USA
SO   Journal of Medicinal Chemistry (1999), 42(18), 3726-3731
     CODEN: JMCMAR; ISSN: 0022-2623
PB   American Chemical Society
DT   Journal
LA   English
AB    (-)Lobeline (1) and (-)nicotine (2) bind at neuronal nicotinic cholinergic
      (nACh) receptors with high affinity (Ki = 4 and 2 nM, resp.).  Previous
      attempts to determine whether lobeline fits the currently accepted nicotinic
      pharmacophore model have led to suggestions that the carbonyl function, rather
      than the hydroxyl group, is a major contributor to binding. Interestingly,
      however, it has never been empirically demonstrated that either oxygen
      function is actually required for interaction with the receptor.  In the
```

present investigation we systematically examined a number of abbreviated analogs of lobeline and found that removal of either one or both oxygen functions reduces the affinity of lobeline by at least 25-fold; furthermore, oxidation of the (-)lobeline hydroxyl group (to afford lobelanine) or reduction of the carbonyl group (to afford lobelanidine) also resulted in decreased affinity. Although it is likely that both oxygen functions contribute to the high affinity of (-)lobeline at nACh receptors, it is concluded that the presence of both oxygen functions is not a requirement for binding; i.e., replacement of the (-)lobeline hydroxyl group with a chloro group had no effect on affinity. Another finding of the present investigation is that removal of either one or both oxygen functions of lobeline results in compds. that retain the analgesic activity and potency of (-)lobeline, indicating that there is no direct relationship between neuronal nicotinic cholinergic (primarily α4β2 type) receptor affinity and spinal analgesia as measured in the tail-flick assay.

IT 246178-16-5P 246178-17-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(lobeline analogs: structure-affinity investigation of neuronal nicotinic receptor binding)

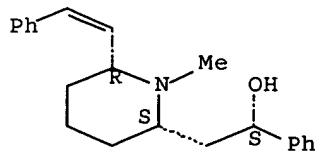
RN 246178-16-5 CAPLUS
CN Ethanone, 2-[(2R,6S)-1-methyl-6-(2-phenylethenyl)-2-piperidinyl]-1-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RN 246178-17-6 CAPLUS
CN 2-Piperidineethanol, 1-methyl-α-phenyl-6-(2-phenylethenyl)-, (αS,2S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

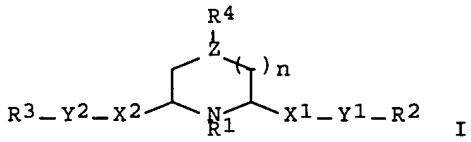
=> s l4 not l5
L6 3 L4 NOT L5

=> dis l6 1-3 bib abs

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:2187 CAPLUS Full-text
DN 142:93692
TI Preparation of 2,6-disubstituted piperidines and piperazines for the treatment of CNS diseases
IN Crooks, Peter A.; Dwoskin, Linda; Jones, Marlon D.; Miller, Dennis Keith; Norholm, Seth Davin; Zheng, Guangrong; Krishamurthy, Sairam
PA USA
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 231,156. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004266824	A1	20041230	US 2004-813647	20040331
	US 6455543	B1	20020924	US 2000-628557	20000728
	US 2003100547	A1	20030529	US 2002-231156	20020830
	US 6943177	B2	20050913		
PRAI	US 1999-146144P	P	19990730		
	US 2000-628557	A3	20000728		
	US 2002-231156	A2	20020830		

OS MARPAT 142:93692
GI



I

AB Title compds. represented by the formula I [wherein X1 = CH2; Y1 = CHOH or C=O; X2-Y2 = cis/trans-carbon-carbon double bond; Z = CH; R1, R4 = independently H or alkyl; R2, R3 = independently (un)saturated hydrocarbon ring or (un)substituted benzene; n = 0-3; and pharmaceutically effective salts thereof, including resolved diastereomers, enantiomers thereof] were prepared For example, lobelanidine was stirred overnight in 85% H3PO4 at 60° to give 78.6% cis-2,6-di-trans-styrylpiperidine. I showed activity in [3H]nicotine binding assay, [3H]MLA binding assay, inhibition of nicotine-evoked 86Rb+ efflux assay, and etc. Thus, I are useful to treat diseases of the central nervous system, drug abuse, and withdrawal therefrom as well as treating eating disorders (no data).

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:723970 CAPLUS Full-text
DN 141:271405
TI Lobeline analogs with enhanced affinity and selectivity for plasmalemma and vesicular monoamine transporters
AU Miller, Dennis K.; Crooks, Peter A.; Zheng, Guangrong; Grinevich, Vladimir P.; Norrholm, Seth D.; Dwoskin, Linda P.
CS College of Pharmacy, University of Kentucky, Lexington, KY, USA
SO Journal of Pharmacology and Experimental Therapeutics (2004), 310(3), 1035-1045

CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Lobeline attenuates the behavioral effects of psychostimulants in rodents and inhibits the function of nicotinic receptors (nAChRs), dopamine transporters (DATs), and vesicular monoamine transporters (VMAT2s). Monoamine transporters are considered valid targets for drug development for the treatment of methamphetamine abuse. In the current study, a series of lobeline analogs were evaluated for affinity and selectivity at these targets. None of the analogs was more potent than nicotine at the [3H]methyllycaconitine binding site (α7* nAChR subtype). Lobeline tosylate was equipotent with lobeline in inhibiting [3H]nicotine binding but 70-fold more potent in inhibiting nicotine-evoked 86Rb+ efflux, demonstrating antagonism of α4β2* nAChRs. Compared with lobeline, the defunctionalized analogs lobelane, mesotransdiene, and (-)-trans-transdiene showed dramatically reduced affinity at α4β2* nAChRs and a 15- to 100-fold higher affinity (Ki = 1.95, 0.58, and 0.26 μM, resp.) at DATs. Mesotransdiene and (-)-trans-transdiene competitively inhibited DAT function, whereas lobelane and lobeline acted noncompetitively. 10S/10R-MEPP [N-methyl-2R-(2R/2S-hydroxy-2-phenylethyl)-6S-(2-phenylethyl)piperidine] and 10R-MESP [N-methyl-2R-(2R-hydroxy-2-phenylethyl)-6S-(2-phenylethen-1-yl)piperidine] were 2 to 3 orders of magnitude more potent (Ki = 0.01 and 0.04 μM, resp.) than lobeline in inhibiting [3H]serotonin uptake; 10S/10R-MEPP showed a 600-fold selectivity for this transporter. Uptake results using hDATs and human serotonin transporters expressed in human embryonic kidney-293 cells were consistent with native transporter assays. Lobelane and ketoalkene were 5-fold more potent (Ki = 0.92 and 1.35 μM, resp.) than lobeline (Ki = 5.46 μM) in inhibiting [3H]methoxytetrabenazine binding to VMAT2 in vesicle prepns. Thus, structural modification (defunctionalization) of the lobeline mol. markedly decreases affinity for α4β2* and α7* nAChRs while increasing affinity for neurotransmitter transporters, affording analogs with enhanced selectivity for these transporters and providing new leads for the treatment of psychostimulant abuse.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:100973 CAPLUS Full-text
DN 134:147501
TI Preparation of cis-2,6-disubstituted piperidines for the treatment of psychostimulant abuse and withdrawal, eating disorders, and central nervous system diseases and pathologies.
IN Dwoskin, Linda P.; Crooks, Peter A.; Jones, Marlon D.
PA University of Kentucky Research Foundation, USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001008678	A1	20010208	WO 2000-US20553	20000728

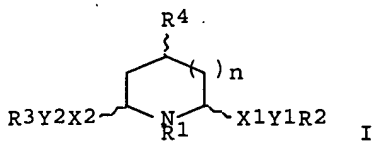
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000063867	A5	20010219	AU 2000-63867		20000728
EP 1513513	A1	20050316	EP 2000-950822		20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
PRAI US 1999-146144P	P	19990730			
WO 2000-US20553	W	20000728			

OS MARPAT 134:147501

GI



I

AB A method for treatment of drug dependence, drug withdrawal, an eating disorder, or a CNS disease or pathol. comprises administration of title compds. [I; n = 0-3; X1Y1, X2Y2 = C-C single, double, or triple bond, C-S bond, C-Se bond, C-O bond, (N-alkyl) C-N single or double bond, N-N double bond; R1, R4 = H, alkyl; R1R4 = atoms to form a ring including CH2, CH2CH2, (CH2)3, cis-CH:CH, cis-CH2CH:CH; R2, R3 = (unsatd.) hydrocarbon ring, N-, O-, S-, and/or Se-containing heterocyclyl, o-, m-, or p-substituted benzene; with provisos]. Thus, lobelanidine was stirred overnight in 85% H3PO4 at 60° to give 78.6% cis-2,6-di-trans-styrylpiperidine. Tested I showed Ki = 0.0043 μM to ≥100 μM in the high affinity [3H] nicotine binding assay.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	15.74	182.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.00	-3.00

STN INTERNATIONAL LOGOFF AT 09:21:17 ON 10 OCT 2006